

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/011300

International filing date (day/month/year)
08.10.2004

Priority date (day/month/year)
09.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61K35/78, A61K31/353, A61P17/00, A61P17/02, A61P35/00

Applicant
MEDIGENE AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Herrera, S

Telephone No. +49 89 2399-8464



Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

801 514 422

International application No.
PCT/EP2004/011300

IAP20 Rec'd PCT/PTO 04 APR 2006

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	30-34
	No: Claims	1-29,35
Inventive step (IS)	Yes: Claims	
	No: Claims	1-35
Industrial applicability (IA)	Yes: Claims	1-35
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section V

1. Reference is made to the following documents:

- D1: WO 2004/026323 A (BARROS, SILVIA, BERLANGA, DE, MORAES;
FUNDACAO DE AMPARO A PESQUISA DO) 1 April 2004 (2004-04-01)
- D2: ZHU A ET AL: "Study of tea polyphenol as a reversal agent for carcinoma cell
lines' multidrug resistance (study of TP as a MDR reversal agent)" NUCLEAR
MEDICINE AND BIOLOGY, ELSEVIER SCIENCE PUBLISHERS, NEW YORK,
NY, US, vol. 28, no. 6, August 2001 (2001-08), pages 735-740, XP004301003
ISSN: 0969-8051
- D3: WO 2004/053097 A (MEDICAL COLLEGE OF GEORGIA RESEARCH
INSTITUTE, INC; HSU, STEPHEN; SCHU) 24 June 2004 (2004-06-24)
- D4: PRONIUK S ET AL: "Preformulation study of epigallocatechin gallate, a
promising antioxidant for topical skin cancer prevention" JOURNAL OF
PHARMACEUTICAL SCIENCES, AMERICAN PHARMACEUTICAL
ASSOCIATION, WASHINGTON, US, vol. 91, no. 1, January 2002 (2002-01),
pages 111-116, XP002270297 ISSN: 0022-3549
- D5: MUKHTAR H ET AL: "GREEN TEA POLYPHENOLS INDUCE APOPTOSIS
AND ALTER THE PROGRESSION OF CELL CYCLE IN HUMAN EPIDERMAL
CARCINOMA CELLS A431" PROCEEDINGS OF THE AMERICAN
ASSOCIATION FOR CANCER RESEARCH AND AMERICAN SOCIETY OF
CLINICAL ONCOLOGY, XX, XX, vol. 38, March 1997 (1997-03), page 580,
XP000997348
- D6: LINDEN K ET AL: "Chemoprevention of non-melanoma skin cancer: Experience
with a polyphenol from green tea" EUROPEAN JOURNAL OF CANCER,
PERGAMON PRESS, OXFORD, GB, vol. 38, February 2002 (2002-02), page
S24, XP004367780 ISSN: 0959-8049
- D7: WO 01/51048 A (COLOR ACCESS, INC) 19 July 2001 (2001-07-19)
- D8: MCCARTY M F: "POLYPHENOL-MEDIATED INHIBITION OF AP-1
TRANSACTIVATING ACTIVITY MAY SLOW CANCER GROWTH BY
IMPEDING ANGIOGENESIS AND TUMOR INVASIVENESS" MEDICAL
HYPOTHESES, EDEN PRESS, PENRITH, US, vol. 50, June 1998 (1998-06),
pages 511-514, XP000957651 ISSN: 0306-9877
- D9: CAO Y ET AL: "ANGIOGENESIS INHIBITED BY DRINKING TEA" NATURE,

MACMILLAN JOURNALS LTD. LONDON, GB, vol. 398, 1 April 1999 (1999-04-01), page 381, XP000953295 ISSN: 0028-0836

D10: US 2003/166583 A1 (YOA-PU HU OLIVER ET AL) 4 September 2003
(2003-09-04)

2. It is already known from the prior art that polyphenols isolated from e.g. green tea, especially derivatives of catechin (or catechol) can be used in the treatment and prevention of different skin disorders, especially skin cancer (cf. D2 and D4 to D10; parts indicated in the search report). The subject-matter of present claims 1 to 29 and 35 therefore lacks the necessary novelty over the prior art and the requirements of Article 33 (2) PCT have not been fulfilled.
3. Since the effect of polyphenols isolated from green tea on cancerous cells is known, it cannot be considered inventive to combine it with other already known agents used for the same indication, especially since no surprising or unexpected effect has been shown. The requirements of Article 33 (3) EPC have therefore not been fulfilled for claims 1-35.

Section VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO2004/026323	01/04/04	17/09/03	18/09/02
WO2004/053097	24/06/04	10/12/03	10/12/02

Section VIII

Certain observations on the international application

The subject-matter of claims 21-26 disclose certain amounts of polyphenols. It is unclear whether these amounts are relative to the complete compositions or relative

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the other active ingredients.